Claim 3 (amended). A recombinant retroviral vector according to Claim 2 wherein said *gag* coding sequence comprises, a splice donor site and a splice acceptor site, wherein said splice acceptor site is located upstream from a [said] gene of interest inserted into said insertion site.

Claim 4, line 2. Replace "gag" with --a--.

Claim 4, line 6. After "comprises", insert --a--.

Claim 6 (amended). A recombinant retroviral vector according to Claim 4 [5], wherein said vector has all of [is MFG having] the identifying characteristics of ATCC 68,754.

Claim 8, lines 3-4. Replace the phrase ", a receptor and a drug." with --, and a receptor.--.

Claim 9, line 2. Replace "is" with --encodes--.

Claim 10 (amended). A recombinant retroviral vector [according to claim 1], said vector [further] comprising:

a) a 5' LTR derived from a retrovirus of interest;

b) a Psi packaging site located 3' to said 5' LTR;

c) an alpha globin transcriptional promoter located 3; to said packaging site;

d) an insertion site for a gene of interest located 3' to said alpha globin promoter;

e) a 3' LTR derived from a retrovirus of interest located 3' to said insertion site; and

f) wherein said vector does not contain a complete selectable marker gene, or a complete *gag*, *env*, or *pol* gene between said 5' and 3' LTRs.

Claim 11, line 3. Replace "α" with --alpha--.

Claim 15 (amended). A recombinant retroviral vector according to claim 14, wherein said vector [is α-SGC and having] has all of the identifying characteristics of ATCC No. 68755.

Claim 18, lines 3-4. Replace the phrase ", a receptor and a drug." with --, and a receptor.--.

Claim 19, line 2. Replace "is" with --encodes--.

Claim 20, line 3. After "any", insert --one--.

Claim 21 (amended). A recombinant retroviral vector comprising [in operable combination], a 5' LTR and a 3' LTR derived from a murine leukemia virus, and an insertion site for a gene of interest located between said 5' and 3' LTRs, wherein said vector does not contain a complete selectable marker gene, or a complete *gag*, *env*, [.] or *pol* gene.

Claim 24, line 2. Replace "Molony" with --Moloney--.

Claim 35 (new). A recombinant retroviral particle which does not encode a complete selectable marker, said particle

having the property of being capable of transducing mammalian cells.

Claim 36 (new). A particle according to claim 35 wherein said transducing occurs *in vitro*.

Claim 37 (new). A particle according to claim 35 wherein said transducing occurs *in vivo*.

SUMMARY OF THE INVENTION

At the time of the present application, one of the major technological obstacles to the genetic manipulation of mammalian cells was the relatively crude methods by which genetic material of interest could be introduced into mammalian cells. In general, prior art methods of introducing genetically engineered nucleic acid into mammalian cells were so inefficient that the primary way one obtained useful quantities of transduced cells was to expand the population of the small fraction of cells that were actually transduced by a lengthy period of selective culturing.

While adequate for many research purposes, the prior art transduction methods, which all involved a lengthy selection process, presented special problems to researchers studying mammalian gene therapy. For instance, many of the differentiated cell types targeted for gene therapy could generally only tolerate relatively short periods of *in vitro* culture, and would not survive the extended periods of selective culture required by the prior art transduction methods.

In addition to the problems encountered with simple *in vitro* culture, problems also ensued where the target cells were organized into histologically distinct structures (i.e., liver, kidneys, etc.). Given that the prior art transduction methods failed to transduce the vast majority of target cells, a majority of the cells in a given tissue sample would perish during selective culture. Needless to say, such massive cell death significantly impacted the integrity, and thus reimplantability, of the target tissues.

The present Applicants recognized, where others did not, that vastly improved vectors would need to be designed and constructed prior to the more widespread application of mammalian gene therapy. As a result of the Applicants' efforts, a novel class of retroviral vectors was constructed which enabled the efficient transduction of virtually any gene of interest[1] into a wide assortment of mammalian cells.

As amended, the present claims are directed the novel class of retroviral vectors developed by the Applicants, the transducing retroviral particles produced therefrom, and methods for using the same. The presently described transducing retroviral particles were used to provide the first demonstration of methods of *in vitro* and *in vivo* transduction which do not require a prolonged selection step.

The amendments to the specification are directed to correcting minor errors of a typographical nature and are not deemed to constitute new matter.

Regarding new claims 35-37, the Specification discusses

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[1]Subject to certain size limitations.

the production of infectious viral particles (from the claimed retroviral vectors) at, *inter alia*, page 17, line 32 through page 18, line 2. As such, the new claims do not constitute new matter.

REMARKS

I. Provisional Double Patenting (and related) Rejections

The Examiner has rejected Claims 5, 6, and 15 under 35 U.S.C. § 101 as claiming the same invention as Claims 6, 15, and 24 of copending U.S. Application Ser. No. 07/786,015 ('015). The Examiner has also rejected claims 5, 6, and 15 as anticipated by the '015 application under 35 U.S.C. §§ 102(e), 102(f), and 102(g). The Examiner has also provisionally rejected claims 1-4, 7-14, and 16-22 under the judicially created doctrine of obviousness-type double patenting. The Examiner has also provisionally rejected claims 23-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the '015 application in combination with Hilberg *et al.* (Hilberg), Holland *et al.* (Holland), Franz *et al.* (Franz), and Weiher *et al.* (Weiher).

Given that the conflicting '015 application has gone abandoned, the Applicants respectfully submit that the above double-patenting rejections have been rendered moot.

II. Rejections based on prior art.

A. Rejections under 35 U.S.C. § 103 in view of the '015 application

The Examiner has rejected Claims 1-4, 7-14, and 16-22 as obvious over the '015 application, and claims 23-31 as

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